A STUDY ON CLINICAL AND BIOCHEMICAL PROFILE IN DIABETIC KETOACIDOSIS

Dissertation submitted in partial fulfilment of the Requirement for the award of the degree of

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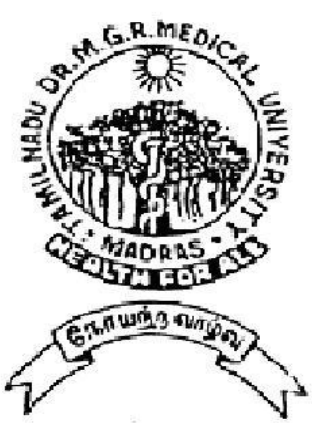

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CERTIFICATE

This is to certify that this thesis entitled “A STUDY ON CLINCAL AND BIOCHEMIAL PROFILE IN DIABETIC KETOACIDOSIS” is a bonafide work of **Dr. SATHIK BASHA.K** for the degree of M.D. General Medicine under my guidance and supervision.

The method of work and the results embodied have been checked by me time to time and are contributory to the knowledge of the subject.

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DECLARATION

I, **Dr. SATHIK BASHA.K,** declare that, I carried out this work on, "**A STUDY ON CLINCAL AND BIOCHEMIAL PROFILE IN DIABETIC KETOACIDOSIS**" at the Department of Medicine, Govt. Rajaji Hospital during the period of April 2012 to November 2012. I also declare that this bonafide work or a part of this work was not submitted by me or any others for any award, degree, and diploma to any other University, Board either in India or abroad.

This is submitted to The Tamilnadu Dr. M. G. R. Medical University, Chennai in partial fulfillment of the rules and regulations for the M.D degree examination in General Medicine.

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ABBREVATIONS

DM- Diabetes mellitus

DKA- Diabetic ketoacidosis

IFG-Impaired fasting glucose

IGT- Impaired glucose tolerance test

LADA- Latent autoimmune mediated diabetes in adults

HLA- Human leukocyte antigen

PCT- Proximal convoluted tubule

S.C- Subcutaneous

I.V- Intravenous

mOsm/kg - Milli osmol/ kilogram

INTRODUCTION

Diabetes mellitus is a metabolic disorder of multiple etiologies, characterized by chronic hyperglycemia with disturbances of carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion, insulin action, or both.

Diabetes mellitus is generally classified into Type 1 and Type2 diabetes. Type1 DM is a complete or near complete insulin deficient state due to autoimmune destruction of pancreatic beta cell. Type 2 DM is due to insulin resistance rather than complete insulin deficient. Here, insulin resistance plays a major role.

The prevalence of diabetes in India in 1970's was 2.3% in urban and 1.5% in rural areas, as shown by the multi-centric study. The prevalence has risen to 12% to 19% in urban areas and to 4% to 9% in rural areas in recent years. (2)

A few population based studies in India indicate the prevalence of retinopathy to be 18% to 27%, overt nephropathy to be about 2.2%, peripheral vascular disease to be 6.3%, peripheral neuropathy to be 26% and coronary artery disease to be about 21%. (2)

Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) are dangerous manifestations of diabetes mellitus representing

two extremes in the spectrum of uncontrolled diabetic state. DKA accounts for 14 percentages of all hospital admissions among diabetics and 16 percentages of all diabetes- related fatalities in India. (2)

DKA occurs predominantly in those with type 1 diabetes. The basic defect in the pathogenesis of DKA is insulin deficiency. Glucagon is a counter regulatory hormone which facilitates gluconeogenesis mechanism, hence hyperglycemia will occur. The absolute insulin deficiency and hyperglycemia leads to synthesis of ketone bodies such as acetoacetate and beta hydroxyl butyrate from hepatocytes, hence ketosis will occur.

The precipitating factors for pathogenesis of DKA are sub optimal insulin dose, insulin or oral antidiabetic drugs omission, respiratory tract infections, genito urinary tract infection, etc and Cerebrovascular accidents such as ischemic stroke and hemorrhagic stroke.

Patients with DKA will present with symptoms of polyuria, thirst, reduction in weight, generalized tiredness, nausea, vomiting, blurring of vision, and abdominal discomfort. Patient may have a signs of dehydration, hypotension, cold extremities, peripheral cyanosis, tachycardia, air hunger (Kussmaul’s breathing), smell of acetone, hypothermia, confusion, drowsiness, and coma.

Most patients with DKA recover when treated properly and if left untreated, patient may develop complications such as cerebral edema, thromboembolism, acute respiratory distress syndrome (ARDS), disseminated intra vascular coagulation (DIC), electrolyte abnormalities, myocardial infarction, infections, and acute circulatory failure.

Early identification ketoacidosis and aggressive management with insulin, intra venous fluids and electrolytes replacement may change the outcome of the disease.

AIMS AND OBJECTIVES

- To study the age and sex distribution in DKA.
- To evaluate the common presentation of Diabetic ketoacidosis.
- To study the precipitating factors of diabetic ketoacidosis.
- To study the role of duration of diabetes on DKA.
- To study the incidence of DKA in poorly controlled diabetes by HbA1c level.
- To study the correlation between serum bicarbonate level and mean duration of hospital stay in DKA patients.
- To study the correlation of HbA1c level and mean duration of hospital stay in DKA patients.
- To study the correlation of serum osmolality and its effect on mental status.
- To study the outcome of DKA patients during treatment.

REVIEW OF LITERATURE

DIABETES MELLLITUS

Diabetes is a metabolic disorder of various etiology characterized by prolonged hyperglycemia with disturbances of carbohydrate, fat, and protein metabolism. It is due to defective insulin secretion, insulin action, or both. The long term complications of diabetes are retinopathy with blindness, nephropathy that may lead to renal failure, neuropathy with foot ulcers, limb amputation, Charcot joints, and autonomic dysfunction like postural hypotension, sexual dysfunction etc. The short term complications of diabetes mellitus are diabetic ketoacidosis and hyperosmolar hyperglycemic state (2). Both are life threatening complications in uncontrolled diabetes.

DIAGNOSIS OF DIABETES MELLITUS

Diabetes mellitus is diagnosed in a person with symptoms of polyuria, polydipsia, polyphagia, recurrent infections, unexplained weight loss and drowsiness, coma with random blood sugar of ≥ 200 mg /dl. (2)

Criteria for diagnosis of diabetes mellitus:

1) HbA1c value more than or equal to 6.5 percentage.

2) Fasting plasma glucose more than or equal to 126 mg/ dl.

3) Random plasma glucose more than or equal to 200 mg/ dl with polyuria, polydipsia, and polyphagia.

4) Glucose tolerance test is categorized in to three classes based on the fasting plasma glucose:

1. Fasting plasma glucose less than 100 mg / dl is considered normal.

2. Fasting plasma glucose ≥ 110 to ≤ 126 mg/ dl (venous plasma) is defined as impaired fasting glucose (IFG).(2)

3. Fasting plasma glucose more than 126mg /dl warrants the further investigation to diagnose diabetes.

4. Depending on the glucose tolerance test, impaired glucose tolerance (IGT) is defined as plasma glucose value between 140 and 199 mg/ dl (2 hour after 75 grams oral glucose intake) and plasma glucose more than 200 mg / dl (2 hour after 75 grams oral glucose intake) is diagnosed as diabetes (2). Individuals with impaired fasting glucose and impaired glucose tolerance test are recently designated as ‘pre diabetes’ by the American Diabetes Association (ADA), are at substantial risk for developing type 2

DM. (1)

Regular exercises, diet advice regarding intake of balanced, low caloric diet, and avoidance of alcohol should be advised in pre diabetic individuals to avoid the further evaluation of diabetes in earlier. (11)

Classification of diabetes mellitus: (2)

Type1diabetes

Type1 diabetes, previously called as juvenile diabetes, is usually identified in adolescents and younger age group. This is due to autoimmune etiology results in destruction of pancreatic beta cells and results in insulin deficient state.

Type 2 diabetes

Type 2 diabetes, previously called as adult onset diabetes. It is a common form of diabetes and has an insidious onset. Type 2 patients are asymptomatic for many years. This is usually occur in adults, but can occur in childhood also. Weight loss is unusual unless the blood sugar is very high. Diabetic ketoacidosis is uncommon in type 2 DM. The incidence of familial inheritance is more common.

Type2 diabetes begins with insulin resistance, and in the initial stage, there is counter regulatory hyperinsulinaemia. In later stage, the pancreas loses its capability to secrete required insulin in response to meal intake and results in clinical diabetes.

Gestational diabetes

It is state of carbohydrate intolerance resulting in hyperglycemia with onset or first diagnosed during pregnancy. Sometimes, carbohydrate intolerance may be unnoticed by the patient before antenatal period and diagnosed first time during pregnancy. In these types of diabetics, regular exercises and weight reduction in obese individual should be advised after delivery, to avoid type2 diabetes in later period.

In these diabetic patients, blood sugar should be estimated six to twelve week after postpartum period to identify the level of sugar control, and after that, it should be monitored every year for life long period.(11)

Among these types of diabetic women about 60 percentages of patients may become diabetic in next five to ten years. The risk of onset of type 2 diabetes is very high in this type.

Latent autoimmune diabetes in adults (LADA):

In this type of diabetic patients have mild or moderate high blood sugar. In early period of the disease, these patients well respond to oral drugs, but in later periods, they will only respond to insulin therapy. These types of diabetics have auto antibodies and if they have more than one auto antibodies, they will become insulin dependent earlier.(11)

Other types of diabetes (2)

The following other type of diabetes exist which occur due to:

- Genetic defects in insulin action,
- Genetic defects of the pancreatic beta cell
- Diseases of the pancreas
- Excess amounts of counter regulatory hormones
- Infections
- Rare autoimmune disorders, and
- Genetic syndromes associated with diabetes.

Etiology and risk factors of DM

Both type1 and type 2diabetes has genetic and environmental risk factors. Type1 diabetes is associated with HLA DR3 and DR4 predisposition. Some possible mechanism of diet and viral infection triggering an autoimmune exposure resulting in destruction of pancreatic beta cell has been identified.(2)

Type2 diabetes has strong genetic basis, as evidenced by its hereditary nature. But the major genes responsible for genetic inheritance have not been identified till date. Asian population was identified as more prone for racial predisposition. Increasing age, obesity, sedentary lifestyle, insulin resistance, and intrauterine adverse environment are other environmental factors associated in the pathogenesis.

Epidemiology of diabetes mellitus

Type 1 diabetes

The estimated global number of type 1 diabetes patients under the age of fourteen years is approximately 4.8 lakhs and approximately seventy six thousand children develop the disease annually. In developing countries like India, the available data is inadequate. (2)

Type 2 diabetes

The worldwide burden due to diabetes is mainly contributed by type 2 DM which include eighty to ninety five percent of the all diabetic population. The disease prevalence is increasing explosively in the past three decades. It was estimated that about two eighty five million adults were affected by the disorder in 2010 and its prevalence will increase to four thirty eight million in 2030.(2)

Type2 diabetes in children

In Asian population, the onset of type 2 diabetes in younger age was increased in recent decades. In Indian children, microvascular diabetic complications were identified even at the time of diagnosis or within a short period after treatment.(2)

type 1 diabetes mellitus - pathogenesis

The following factors are responsible for the pathogenesis of type 1 diabetes

- Genetic factors
- Environmental triggers
- Pancreatic beta cell destruction by various factors.

Genetic factors

In recent studies, familial clustering of type1 diabetes with siblings of type 1 patients having a risk of five percent and the risk of transmission from parents is about ten percent.

HLA class I and II encoding genes are situated within the HLA region of chromosome 6. In some studies, the high incidence of type 1 diabetes with HLA-B8 and no or low incidence with HLA-B7 were identified. The risk was very high with HLA class II namely DR3 and DR4. DR2 was identified as protective.

Environmental factors

Viruses

Viruses can affect pancreatic beta cells directly by cytolytic effects or indirectly triggering autoimmune response. In children with mumps virus infection develop antibodies against islet cell suggesting underlying autoimmune processes. Coxsakievirus B, cytomegalovirus, Epstein-Barr virus, and retro virus are all associated with type 1 diabetes.

Dietary factors

Type1 diabetes incidence was reported high in population were the drinking water contains high amount of nitrites and nitrates. Consumption of smoked and cured mutton also associated. Early exposure to cow milk in infants was another factor responsible for high incidence of type 1 diabetes. Vitamin D supplementation was identified as protective against type1 diabetes.

Auto immune damage to beta cells

Fifty to ninety percent of type1 diabetes patients had antibodies against islet cells, and glutamic acid decorboxylase. Type1 diabetes is associated with autoimmune diseases like Hashimoto's thyroiditis, Grave's disease and celiac disease, etc.

Pathogenesis of type 2 diabetes

The pathogenesis of type 2 diabetes is mainly due to two important factors. These are

1) Peripheral insulin resistance and Hepatic insulin resistance
2) Impaired beta cell function(insulin secretory defect)

Peripheral and hepatic insulin resistance

It was first described in obese type2 patients. Even though, the insulin level is high in type 2 diabetic patients, there is low glucose utilization and insulin inaction in the adipose tissue, muscle and hepatic cells. The molecular mechanism underlying the insulin resistance is prolonged hyperglycemia, produces glucotoxicity, due to failure to enhance hexosamine pathway, leading to increased glucosamine levels. This increased glucosamine level produce insulin resistance in adipose tissue and other tissues.

Another mechanism is prolonged hyperglycemia will down regulate the insulin receptor and further worsen insulin resistance. The glucocorticoid induced insulin resistance is also identified as a pathogenic factor.

Insulin secretory defects

In a normal person, about eighteen to thirty units of insulin is secreted daily and about fifty percent is removed from the liver for local action during its first passage. In type 2 diabetes, both rapid meal related insulin secretion which occurs within 30 minutes after meal, and post meal insulin secretion which occurs for the 2 hour period are impaired. The molecular mechanism responsible for these changes is due to over expression of hexokinase genes as

compared to glucokinase gene.

The beta cell mass is minimally reduced at the time diagnosis and the disease progress to several years, the beta cell mass declines further due to fibrillary amylin deposition in the beta cells.

In about ten percent of type 1 diabetics, the beta cell failure is due to auto immune process. This is known as latent autoimmune diabetes of adults.

Incretin effect in the pathogenesis of type2 diabetes

The gastrointestinal tract secretes the hormones called incretins. This includes glucagon like peptide and glucose dependent insulinotropic peptide. These hormones are responsible for the increased secretion of insulin after oral glucose intake. This is known as incretin effect. This effect is blunted in type 2 diabetes.

Other mechanism is high glucagon level after meal also responsible for hyperglycemia.

Hypothalamic neurons and neurotransmitters are identified in pathogenesis type 2 diabetes. The first phase of insulin secretion is mediated through these pathways. In obese and insulin resistant subjects, after the glucose intake, the elevated plasma insulin

levels are unable to produce inhibitory response in these nuclei.

Role of kidney in pathogenesis of type2 diabetes

In a normal individual, about 160 gram of glucose is filtered in the glomerular filtrate. About ninety percent of it is reabsorbed in PCT by glucose transporter called SGLT2. Another ten percent of the filtered glucose is absorbed in the descending part of proximal tubule by glucose transporter SGLT1. In type2 diabetes, the SGLT2 is increased up to four times of normal. This leads to increased glucose resorption and hyperglycemia.

HbA1c level and its importance

HbA1c level is a glycosylated hemoglobin level in plasma and its level increases with poor control of blood sugar in diabetic individuals. HbA1c level and its interpretation

Normal = less than 5.7 percentage

Pre-diabetes = 5.7 to 6.4 percentage

Diabetes = 6.5 percentage and more

Diagnosis based on HbA1c needs confirmation by routine blood sugar methods. In asymptomatic individuals with HbA1c level

more than 6.5 percent, if pre prandial blood sugar >126 mg/dl or random blood sugar >200 mg/ dl, diagnosis of diabetes is confirmed.

The advantage of HbA1c measurement:

1) Patient need not to remain fasting.
2) HbA1c level is a measure of long- term plasma glucose control, rather than present plasma glucose.
3) Errors due to other factors affecting HbA1c like haemoglobinopathies can be minimised by comparing plasma glucose level.

In patients with high HbA1c level, the metabolic control is poor, leads to chronic hyperglycemia. In this situation, single dose of insulin or drug omission, and infection may trigger the development of ketoacidosis or hyperosmolar hyperglycemic state in diabetes.

The lack of availability of HbA1c test in remote areas, the high cost of the test, and faulty standardization techniques are certain limitations in using this test. Non glycemic factors modifying HbA1c level such as anemia, polycythemia, haemoglobinopathies

and uremia are other limitations of this test.

DIABETIC KETOACODOSIS

Diabetic ketoacidosis (DKA) and Hyperosmolar hyperglycemic state (HHS) represent two distinct metabolic derangements manifested by insulin deficiency and severe hyperglycemia.

DKA occurs in the setting of more severe insulin deficiency, and low circulating levels of insulin leads not only to hyperglycemia and dehydration but also to the production of ketone bodies and acidosis.

HHS occurs when insulin deficiency relative to insulin requirements causes hyperglycemia, which in turn leads to dehydration, resulting in a severe hyperosmolar state.

To diagnose the DKA, the following are essential:

1) High blood sugar (blood sugar more than 250 mg / dl)[13]
2) Ketosis
3) Acidemia (pH less than 7.3)

Sometimes, both diabetic ketoacidosis and hyperosmolar hyperglycemic state can occur simultaneously.

EPIDEMIOLOGY

In one of the largest studies of the epidemiology of DKA, Faich et al reported an annual incidence of DKA in Rhode Island of 46 cases per 10,000 persons with diabetes and 1.4 cases per 10,000 persons in the general population. (13)

More than twenty percent of patients admitted for DKA had previously undiagnosed diabetes. Another fifteen percent of admissions were of patients with multiple admissions for DKA.

Several studies reported that the average age of patients admitted for DKA was 40 to 50 years, but that the risk decreased with age.

Some studies have reported a female predominance possibly because young women were more likely to have repeated episodes of DKA. (13)

DKA is the one of the major cause of death in diabetic individuals, younger than 24 year old, accounting for about one half of the deaths in this population group. Before the discovery of insulin in 1921, the mortality due to DKA was virtually 100%. By 1932, mortality decreased to 29%.

By the 1950s, the reported mortality was 15%, with the improvement

credited primarily to the widespread use of antibiotics, the intra venous potassium replacement, and the use of norepinephrine for blood pressure support.

In recent studies, mortality rate was ranging from 2.5% to 9% **among patients admitted with DKA have been reported. Mortality** among patients with DKA has been related to age, degree of hyperosmolarity, and severity of azotemia.

PATHOPHYSIOLOGY OF DKA:

In both diabetic ketoacidosis and hyperosmolar hyperglycemic stare, relative insulin deficiency is the critical underlying defect. In both DKA and HHS, sub optimal level of insulin in peripheral circulation relative to insulin requirements results in hyperglycemia, further results in total body water deficit. When insulin deficient state becomes severe, ketoacidosis will occur.

Type 2 diabetics develop ketoacidosis even without insulin deficient state due to presence of insulin resistance. Insulin resistance is mediated by several factors, including the pathophysiology of type 2 diabetes and increase in the level of counter regulatory hormones, including cortisol, glucagon, epinephrine, and growth

hormone.

Any physiologic stress in the patient with type 1 diabetes may result in DKA, due to elevated levels of counter regulatory hormones.

insulin Deficiency

↓ ↓

Increased lipolysis **hyperglycemia**

↓ ↓

Increased ketogenesis **Osmotic Diuresis**

↓ ↓

Ketoacidosis **Hyperosmolarity**

↓ ↓

Pure diabetic

Ketoacidosis ↔ **Pure Hyperosmolar state.**

The role of counter regulatory hormones in the pathogenesis of diabetic ketoacidosis:

1) Increased secretion epinephrine, cortisol, and growth hormone inhibits the insulin facilitated glucose utilization in the muscles, there by hyperglycemia and ketosis.
2) High levels of glucagon and other hormones results in activation gluconeogenesis mechanism and glycogen breakdown mechanism in the hepatocytes, thereby

hyperglycemia will occur.

3) Epinephrine and growth hormone facilitate the lipid breakdown mechanism in the fat tissues.
4) Epinephrine and growth hormone may have direct effect on inhibition of residual insulin secretion.

In diabetic ketoacidosis, the relative or complete insulin deficiency and counter regulatory hormone like glucagon excess leads to gluconeogenesis and ketone body synthesis from the liver. The marked elevation in free fatty acid release from the adipocytes secondary to reduced insulin level and increased ketone body synthesis (acetoacetate and beta hydroxybutyrate) from the liver through activation of carnitine palmitoyltransferase I secondary to high glucagon level, results in ketosis. This carnitine palmitoyltransferase I enzyme is responsible for the fatty acid transport into the mitochondria. In mitochondria, beta oxidation and conversion to ketone bodies occurs. These ketone bodies have a low pH and result in metabolic acidosis.

In Hyperosmolar hyperglycemic state, some amount of insulin is available for ketosis prevention but the amount of available insulin to control hyperglycemia is not optimum, is the reason for

absence of ketosis. Hyperosmolar state itself decreases the amount of free fatty acids available for ketogenesis. In addition, low counter regulatory hormones found in hyperosmolar state also prevent the ketosis formation.

Gerich et al studied the effects of infusing counter regulatory hormones in to insulin-dependent patients. Neither glucagon nor did growth hormone infusion produce an elevation in ketone bodies until insulin was withdrawn.

The hyperglycemia causes a profound osmotic diuresis leading to dehydration and electrolyte loss, particularly of sodium and potassium.

In an adult diabetic ketoacidosis patient, approximately about six litters of water, 500 mmols of sodium, 400 mmols of chloride, and 350 mmols of potassium will be lost.

About half the deficit of total body water is derived from the intracellular compartment and occurs comparatively early in the development of acidosis with relatively few clinical features; the remainder represents loss of extracellular fluid sustained largely in the later stages. It is at this time that marked contraction of the

size of the extracellular space occurs, with haemoconcentration, a decreased blood volume, and finally a fall in blood pressure with associated renal ischemia and oliguria.

Every patient with diabetic ketoacidosis will be in a state of potassium-depleted, but the plasma concentration of potassium gives very little indication of the total body deficit.

Plasma potassium may even be raised initially due to disproportionate loss of water and catabolism of protein and glycogen. However, soon after insulin treatment is started there is likely to be a precipitous fall in the plasma potassium due to dilution of extracellular potassium by administration of intravenous fluids, the movement of potassium into cells as a result of treatment with insulin, and the continuing renal loss of potassium.

The sodium concentration is increased due to hyperglycemia in ketoacidosis. So, in DKA, the normal sodium level denotes that water deficit is much severe.

The serum osmolality is measured by = 2× Na + Blood sugar /18 + Blood urea / 5.6.

The normal serum osmolality is between 285- 295 mOsm/ kg. The

linear relationship was noted between the patient's serum osmolality and their mental alteration in several studies. Serum osmolality can be increased mildly in DKA.

The differentiating features between diabetic ketoacidosis and

Hyperosmolar state

		Diabetic ketoacidosis	Hyperosmolar hyperglycemic state
1	Blood sugar	More than 250 mg /dl	More than 600 mg / dl

2	pH	Less than 7.2	More than 7.4
3	Bicarbonate level	Less than 15 mEq/ l	More than 15 mEq/ l
4	Serum/ urinary ketone	Positive	Negative
5	Serum osmolality	Variable	More than 320mOsm /kg
6	Anion gap	More than or equal to 13	Less than 12
7	Mental confusion	Depends on severity	Stupor or coma is common

During ketone body production, hydroxybutyrate is produced more than three times of acetoacetate. Nitroprusside reagent method detects acetoacetate in urine. But, measurement of hydroxybutyrate in blood is ideal method, because it denotes the real ketone body level in the blood.

Precipitating factors in DKA are

- Sub optimal insulin dose.[1,2,3,13)]
- Insulin or anti diabetic drug omission.
- Respiratory tract infection, urinary tract infection, wound infection etc.
- Cerebrovascular accidents such as ischemic stroke and hemorrhagic stroke
- Myocardial infarction
- Uncontrolled diabetes.
- Antenatal period.

Complete omission or inadequate administration of insulin by the patient may precipitate DKA. Patients using insulin infusion pump

devices with short-acting insulin may develop DKA within few hours, if the fault occurs in devices.

About 20- 40 percent of DKA is precipitated by infection. Among the infections, urinary tract infection and respiratory tract infection are more common. (1, 3)

Cerebrovascular accidents, myocardial infarction, pancreatitis, and alcohol abuse are rare causes of precipitating factors, account for about 10 % of all cases of DKA. (1, 2, 3, 13).

In adolescent population, the most common precipitating cause is omission of insulin, because many of whom utilize this as an opportunity to control weight.

Drugs also may precipitate DKA, most offending drugs are corticosteroids, sympathomimetic drugs (dobutamine and terbutaline), and thiazide diuretics. (3)

Recently, newer antipsychotic drugs like clozapine, olanzapine, and risperidone have been identified as the cause for hyperglycemia and DKA. Treatment with interferon-alpha and ribavirin has been associated with the development of DKA in a patient with hepatitis C.

In some patients, the precipitating events could not be identified.

Clinical features:

DKA may be the initial presentation to the hospital to a diagnosis of type1 diabetes and even some with cases of type 2 diabetes. But, DKA is common in patients who are already having diabetes. **The presenting symptoms of DKA are as follows:**

- Polyuria [1, 3]
- Thirst
- Wight loss
- Weakness
- Nausea, vomiting
- Leg cramps
- Blurred vision
- Abdominal pain
- Shortness of breath
- Altered sensorium

The presenting signs are as follows

- Dehydration[1,3]

- Hypotension (postural or supine)
- Cold extremities
- Peripheral cyanosis
- Tachycardia
- Air hunger (Kussmaul breathing)
- Smell of acetone
- Hypothermia
- Lethargy, confusion, drowsiness
- Coma

Nausea and vomiting are most common presentation. So the lab investigations for ketosis should be obtained for patients presenting with the above symptoms. In some patients, abdominal tenderness may mimic like acute abdomen or bowel perforation.

High blood sugar leads to increased amount glucose leak in the urine, may produce dehydration and increased heart rate.

Hypotension is due to decrease in blood volume and dilatation of vessels.

Kussmaul respirations are due to low pH and high amount of ketone bodies.

Hyperglycemia induces the cerebral edema, results in lethargy, confusion, finally coma and death. Cerebral edema, is one of the dangerous complication, is more common in 0- 12 years.

Diagnosis

Laboratory investigations

In patients with symptoms and signs of DKA, the following investigations should be ordered for diagnosis. (13)

- Complete haemogram
- Plasma glucose
- Serum and urine ketones
- Serum electrolytes
- Blood urea
- S.Creatinine
- Arterial blood gas
- Electrocardiogram
- Cultures of urine, blood and throat – if clinically indicated
- Chest X ray- if respiratory infection is under suspicion
- HbA1c (glycosylated hemoglobin)- may provide information about the degree of metabolic control.

In patients with severe dehydration, serum Na level is elevated. The acidosis leads to a shift of intracellular potassium to extracellular. So, serum potassium level may be high at presentation. When treatment is started, potassium replacement is required, because resolution of acidosis will lead to cellular reuptake of potassium and hypokalemia. When potassium value at the time admission more than 5.5mEq/l , or due other associated renal injury, potassium infusion is not warranted. If the hypokalemia during insulin therapy is not corrected, may result in cardiac arrhythmia.

Patient's serum osmolality values are sometimes responsible for their mental confusion / coma. If the patient is presenting with coma and altered sensorium, with osmolality < 320 mOsm/kg, possibilities of other causes of com should be suspected.

Without the presence of pancreatitis, the pancreatic enzymes can be elevated. Increase in pancreatic enzymes more than three times of normal do not confirm a diagnosis of pancreatitis in these situations. Sometimes, coexisting pancreatitis may be present in 10% - 15% of patients with DKA.

Leukocytosis may occur in DKA in the absence of infection. The mechanism of leukocytosis is not clearly understood.

Differential diagnosis

Other causes of ketoacidosis need to be considered when diabetic patient present with ketosis. These include

- Starvation ketosis
- Alcoholic ketoacidosis
- Uremia in chronic kidney disease
- Drugs producing metabolic acidosis

Treatment of diabetic ketoacidosis

Treatment of DKA is based on correcting the underlying the pathophysiologic defects, correcting the fluid and electrolyte imbalance, normalizing the blood glucose, correcting the acid base disturbance, and treating the precipitating cause.

Fluids

Normal saline should be given at rate of 15 ml per kilogram per hour and followed by 0.45 percent normal saline at a rate of 250 ml per hour. When blood sugar reaches below 250mg/dl, 5 percent

dextrose solution should be changed.

Guidelines for insulin management

- Regular insulin 10 U i.v bolus [1,13]
- Followed by regular insulin at a dose of 0.1 Units per kilogram per hour should be given in infusion.
- Increase insulin 1 U per hour every 1-2 hour if less than 10 % decrease in blood sugar.
- When blood sugar comes down to less than 250 mg/dl, the insulin dose should be reduced 1 to 2 units per hour.
- Maintain blood sugar between 140 – 180 mg/ dl.
- When the blood sugar comes down below 80 mg / dl, insulin should be stopped for sometimes.
- If the blood sugar level is below 100 mg/dl for long time, dextrose containing fluids should be given.
- Once the patient is able to eat, change to subcutaneous insulin. Overlap short-acting insulin s.c and continue i.v infusion for 1-2 hours.

For patients with previous insulin- return to previous dose of insulin.

For patients with newly diagnosed diabetes: full dose s.c insulin based on 0.6 U/kg per day. (1,13)

Replacement of potassium

When plasma k+ level is < 5-5.2 mEq/ Littre, 10 mEq of potassium is replaced per hour. If the K+ less than 3.5 mEq / Litre, 40- 80 mEq of potassium should be replaced. If the initial serum potassium is > 5.2 mmol/Littre, potassium should not be given. Once the K+ level come down to normal limits, K+ replacement can be given. (13)

Bicarbonate supplementation

In most situations, treatment with insulin results in resolution of the acid-base abnormality. No studies to date showed the benefits of bicarbonates replacement. So, treatment with bicarbonate should be considered only in patients whose pH is < 7.0. It should be given intravenously in a dose of 100 ml of Sod. Bicarbonate in 500 ml saline; 200 ml per hour.

During management, capillary glucose should be monitored every 1-2 hours. Serum electrolytes especially potassium, bicarbonate should be measured every 4 hours for first 24 hours.

In recent days, early identification of DKA by lab investigation, and prompt initiation of treatment in intensive care units has reduced the mortality rate to less than 1 percentage in developed countries.

But, in developing countries, still the mortality rate is high.

Phosphates and magnesium:

In DKA patients, phosphate and magnesium level are decreased and further reduction may occur during insulin treatment. But, usually, these electrolytes are not given, when the patient takes oral diet. If the phosphate level is low, and the patient is not taking oral diet, potassium phosphate can be given. (11,13)

If magnesium level found low level in DKA patient, who developed cardiac arrhythmias, magnesium sulfate can be given. Otherwise, routine supplementation is not needed.

Complications of diabetic ketoacidosis:

Metabolic complications occurring while treatments are electrolyte abnormalities (hypokalemia / hyperkalemia), sudden hypoglycemia, and rarely hypocalcaemia.

Infection may be aggravated due to uncontrolled diabetes during treatment.

Hypovolemic shock can occur due to severe dehydration and sepsis.

Vascular complications like cerebral thromboembolism can occur due

to dehydration.

Acute pulmonary edema of non cardiac etiology can occur due excess fluid replacement, especially in patients with associated co morbid illness.

Increased intracranial tension and cerebral edema can occur if acidosis is severe.

Lactic acidosis may be precipitated in some DKA patients.

If insulin is stopped earlier before the disappearance of ketoacidosis, rebound ketoacidosis may occur and may worsen the outcome of the disease.

Prevention aspects in DKA:

Diabetic patient should be educated about the importance and seriousness of the disease.

Self monitoring of blood sugar is advised all diabetic, to achieve a target blood sugar. Especially who are on insulin, should be advised self blood sugar monitoring twice a day.

Continuous blood sugar monitoring in patients with wide variability in blood sugar level, can be advised.

HbA1c level can be monitored once in three months, to know the long term blood sugar control.

Routine monitoring of urine acetone in type1 patients with the use of ketostix can be advised for earlier identification of DKA. (11)

Review of other relative studies in diabetic ketoacidosis:

Daad Hassan Akbar conducted a study in King Abdul Aziz university hospital, Saudi Arabia, in 102 Diabetic ketoacidosis patients. In this study, 75 percentages of patients were type1 diabetes and 25 percentages of patients were type 2 diabetes. Male: female sex ratio was 2.1: 1. In this study, poor compliance and sub optimal insulin dosage was the major precipitating factors (56 percentages). The major presenting problem in this study was nausea and vomiting (89 percentages).

Berhane Seyonum, MD was conducted a study in University school of Medicine, Detroit, among the 847 DKA patients. In this study 17 percentage of DKA patients were newly diagnosed diabetes. Among these 847 patients, 311 patients (36%) were repeatedly

admitted for diabetic ketoacidosis. Males were more affected than females in a ratio of 2:1. 59 percentages of patients were admitted for discontinuation of treatment and infection was the next cause for development of ketosis (38 percentages). The average mean duration of hospital stay in this study was 6.7 days. Among these study population, the mortality rate was 6%.

C Rajasoorya and his colleagues had done a study among 33 DKA patients in Department of medicine, Alexander hospital, Singapore. In this study, 18 percentages were newly detected diabetes. 52 percentages of the patients were presented with polyuria and polydipsia. In this study the mean serum osmolality value was correlated in patients who presented with confused state or coma and found that it was higher in patients with confused state than in patients presented with other symptoms. Among the precipitating causes, infection remained the primary cause for development of DKA. The mortality rate in this study was 10 percentages.

Ramaswamy Ganesh and his colleagues did a comparison study among 21 children in Department of pediatrics, Kalawati saran hospital, Delhi. Among these 21 patients 13 were boys and 8 were girls (sex ratio was 1.4: 1). He observed that the HbA1c level was

very high in all 21 patients and 17 percentages of patients were presented with polyuria.

Balasubramanyam A et al, from Department of Medicine, Baylor college of Medicine, Houston had done a cross sectional study in 141 DKA patients. Among these patients, 53 % were type 1diabetes, 39 % were type 2 diabetes and 8 % of the patients were could not be identified as either type1or type 2 DM. Type 1 diabetes were relatively lean and mean age of diagnosis of diabetes in type 1 patients was less than 40 years.

In Department of Endocrinology, Post graduate institute, Chandigarh, Matoo V K and his colleagues, did a prospective study among 143 DKA patients over a period of 6 years. The result showed that 48 patients were newly diagnosed as diabetes with ketoacidosis. Among these 143 patients, 42 patients were presented with infection (30 percentages). During this study, 34 patients died due to DKA complications (23.7 percentages). The mortality rate was very high in this study.

Qari FA had done a study in university hospital, Saudi Arabia, among the 68 diabetic ketoacidosis patients. In his study, he reported that poor compliance was the major factor for the development of

DKA. The mortality rate in his study was 2.9 percent.

Tahboub I et al, in Jordan did a prospective study in DKA over four years in 147 patients, and he found that 89 patients were male and 78 patients were female. Twenty one percentages of patients were newly detected diabetics in his study. Most the patients developed DKA due to non compliance. The mortality rate due to diabetic ketoacidosis in that institution was about 4.8 percentages.

Habib HS did a study in 2005, at king university, Jeddah, among the 172 children. Among these patients, 101 were female children and 71 were male children. In this study, DKA incidences were more in female children. Among the study population, 21 children were having altered consciousness. He correlated the patient's acidosis level and their mental confusion and presentation with coma. He reported that, the patient's acidosis level at the time of admission was significantly correlated with their mental confusion state.

Snogaard O et all had done a study in 1989, among the 175 diabetic patients admitted with ketoacidosis. In this study, he observed that diabetic patients were repeatedly getting admission for ketoacidosis and the recurrence rate; he reported was around 3.4 percentages.

Akhter khan et al conducted a study, in Aga khan university, among the 62 patients of DKA. Among these patients, 44 (71 percentages) were type 1 diabetics and 18 (29 percentages) were type 2diabetics. Infection was the primary cause to precipitate diabetes about 45.2 percentages. He correlated the neurological status with patient's random blood sugar mean, pH level and serum osmolality level. He observed that the mental alteration in patients who were having high random blood sugar, low pH and high serum osmolality values at a statistically significant level.

MATERIALS AND METHOD

Study design: prospective study.

Selection of study population:

This cross sectional study includes 50 patients with Diabetic ketoacidosis admitted in medicine ward and Intensive care unit in Government Rajaji Hospital, Madurai.

Type 1 and type 2 diabetic patients of both sexes were included in the study. Both symptomatic and asymptomatic patients were included in the study.

The study includes both newly detected diabetic ketoacidosis patients as well as patients who were already receiving diabetic treatment, developing diabetic ketoacidosis. The written informed consent was obtained from each patient or his / her relatives about the study.

Period of study: 9 months.

Collaborative departments:

1. Department of Diabetology, GRH, Madurai.
2. Department of Biochemistry, GRH, Madurai.

Biochemical investigations:

The initial biochemical investigations such as Random blood sugar, Serum Elecrolytes (Sodium, potassium, and bicarbonate), Urine Acetone, Blood urea, and Serum Creatinine were measured to confirm the diagnosis.

Urine ketone bodies were identified by Rothera's nitroprusside test. This test procedure was as follows,

1) Preparing the reagent by mixing 10g ammonium sulfate, 0.3g sodium nitroprusside and 5g anhydrous sodium carbonate.
2) 0.5 – 1.0g of this reagent was taken in to a test tube and a drop of fresh urine was added.
3) The color change after 1 minute was observed. Under alkaline condition, ketone bodies react with nitroprusside to give a purple color ring.

HbA1c level was measured by automated analyzer method.

The presenting symptoms such as Nausea/vomiting, mental confusion, Thirst / polyuria, Wight loss / weakness, abdominal pain, Coma and without symptoms were elicited by history and clinical

examination to evaluate the common mode of presentation.

The precipitating factors for the diabetic ketoacidosis such as, in adequate insulin administration, Poor patient compliance, Infection, Infarction, and without obvious precipitating cause were assessed by history and clinical examination to find out the common precipitating factor.

Duration of diabetes:

The duration of diabetes is recorded for each patient by history and available records. According to the duration of diabetes, the study group is divided in to four groups.

1) 0 – 5 years of duration of diabetes.
2) 6 – 10 years of duration of diabetes.
3) 11 – 15 years of duration of diabetes.
4) More than 15 years of duration of diabetes.

These 4 four groups were compared to evaluate, whether the incidence of DKA increases with increased duration of diabetes.

HbA1c level:

In all the study patients, HbA1c level was measured by automated analyzer method to find out the past 3 month duration of glycemic control. In this study DKA patients were divided in to four groups

based on the HbA1c level.

Group I – HbA1c level between 6.5-7.5 %

Group II- HbA1c level between 7.6-8.5%

Group III- HbA1c level between 8.6-9.5%

Group IV - HbA1c level more than 9.6 %

These four groups were compared to find out the role of long standing poor glycemic control for development of diabetic ketoacidosis.

In these four groups the mean duration of hospital stay was calculated separately to find the effect of HbA1c level in outcome of the DKA patients.

Serum osmolality:

The serum Osmolality was calculated from the following formula:

2 × Na + Blood sugar /18 + Blood urea / 5.6.

The normal range of serum osmolality is 285-295 mOsm/kg. Studies on serum osmolality and mental alteration have established a positive linear relationship between osmolality and mental alteration.

In this study, study groups were divided in to two groups according to their serum osmolality.

Group A: Serum Osmolality less than 320 mOsm/ kg

Group B: Serum Osmolality more than 320 mOsm/kg

In each group, number of patients had the altered level of consciousness, and coma during presentation or during treatment was counted. These values were compared among these groups to find out the relationship between the serum Osmolality and mental alteration and outcome in DKA patients.

Serum bicarbonate level:

In this study, patients were divided in to three groups according to their serum bicarbonate values.

Group I = serum bicarbonate level between 16-20mEq/l.

Group II = serum bicarbonate level between 11-15mEq/l.

Group III = serum bicarbonate level ≤ 10mEq/l.

In these three groups, the mean duration of hospital stay was calculated separately and these values were compared to find the correlation of serum of serum bicarbonate level and outcome of the

patient.

Results and observation of the study

Age distribution:

Among these 50 DKA patients, 7 patients were in 13- 20 years age group (mean age =16.2 and 14%), 13 patients were in 21- 30 years age group (mean age =26.02 and 26%), 11 patients were in 31-40 years age group (mean age = 33.14, and 22 %), 6 patients were in 41- 50 years age group (mean age = 45.08 and 12%), 8 patients were in 51 - 60 years age group (mean age = 54.04 and 16 %) and 5 patients were in more than 60 years age group (mean age = 68.20 and 10%). These data reveal that the incidence of DKA was higher in 21- 40 years in an adult population.

(Table-1and chart-1)

Sex distribution:

In this study, 36 patients were male (72%) and 14 patients were female (28%). This result shows that DKA is common in male population compare to female population. (Table-2 and Chart-2)

Incidence of DKA among type1 and type 2 diabetes patients:

In our study, among these 50 patients, 31 patients were belongs to type 1 diabetes and 19 patients were belongs to type 2 diabetes. It clearly

shows that the incidence of diabetic ketoacidosis was more common in type 1 patients. (Table- 3 and chart- 3)

Duration of diabetes and incidence of DKA:

In this study, 22 patients had 0-5 year duration of diabetes, 14 patients had 6- 10 year duration, 12 patients had 11- 15 year duration , and only 2 patients had more than 15 year duration of diabetes. This result shows that the more duration of diabetes and incidence of Diabetic ketoacidosis didn't have the correlation. (Table-4 and Chart-4)

Presentation of DKA patients:

Among these 50 patients, 13 patients were presented with symptoms of thirst and dehydration (26%), 11 patients were presented with mental confusion(22%), 7 patients were presented with nausea and vomiting (14%), 3 patients were presented with hypotension and cold extremities (6%), 2 patients were presented with shortness of breath (4%), 3 patients were presented with abdominal pain (6%), 3 patients were presented with lethargy (6%), 2 patients presented with palpitation and tachycardia (4%), 2 patients were presented with coma (4%), and 4 patients were diagnosed incidentally with high blood sugar with no symptoms(8%). This result shows that the thirst and dehydration, mental confusion, and nausea and vomiting were the

common presenting problems in diabetic ketoacidosis. (Table-5 and Chart-5)

Precipitating factors identified in DKA patients:

In our study, infections such as urinary tract, respiratory tract, and wound infection were identified in 17 patients as a precipitating cause (34%), insulin or drug omission was the cause in 14 patients (28%), inadequate insulin administration was the cause in 7 patients (14%), cerebral infarction was the cause in 2 patients (4%), and in 8 subjects, no cause was identified for precipitation DKA (16%). Two patients were newly diagnosed as diabetes and the initial presentation was DKA (4%). (Table-6 and Chart6)

DKA incidence and correlation with HbA1c level:

In this study, 5 patients had HbA1c value of 6.5-7.5 (10%), 9 subjects had HbA1c level of 7.6-8.5 (18%), 12 patients had HbA1c level of 8.6-9.5 (24%), and 24 patients were having HbA1c value more than 9.5 (48%). These values shows that incidence of diabetic ketoacidosis was high in diabetic patients who were having high HbA1c level. (Table-7 and Chart-7)

Correlation of serum osmolality and mode of presentation in DKA patients:

In this study, 37 patients were having serum osmolality values less than 320 mOsm/kg and among these 37 patients, only 3 patients were presented with mental confusion/ coma (8.1%). 13 patients were having serum osmolality values more than 320 mOsm/Kg and among these 13 patients, 11 patients were presented with mental confusion and coma (84.6%). This result shows that positive correlation between higher serum osmolality values and high incidence of mental confusion/ coma in DKA patients. (Table – 8 and Chart – 8)

Outcome of the treatment:

In 50 patients, 47 patients (94%) were completely recovered from DKA and 3(6%) patients were died due to complications. This result shows that the mortality rate was 6 %. (Table- 9 and Chart- 9)

Correlation of serum bicarbonate level and mean duration of hospital stay in DKA patients:

In our study, 31 patients were having their serum bicarbonate values in between 16-20 mEq/L , and the mean duration of hospital stay in these patients was 9.8 days (p value= 0.054). 12 patients were having bicarbonate values in between 11-15 mEq /L, and the mean duration of hospital stay in these patients was 12.06 days (p value = 0.004). In

7 patients, serum bicarbonate values are ≤ 10 mEq/L and the mean duration of hospital stay in these patients is 14.2 days (p = 0.001, statistically significant). These results show that the mean duration of hospital stay was increased in patients with low bicarbonate values. (Table- 10 and Chart -10)

Correlation of patient's HbA1c values with mean duration hospital stay:

In our study, 5 patients were having HbA1c values in between 6.5- 7.5 and mean duration of hospital stay in these patients was10.02 days (p value= 0.504, not significant). In 9 patients, the HbA1c values were in between 7.6- 8.5, and mean duration of hospital stay in these patients was 10.2 days (p value = .482. not significant). 12 patients were having HbA1c values in between 8.6-9.5 and their mean duration of hospital stay was 10.1 days (p value =0.501, not significant). 24 patients were having their HbA1c values > 9.6 and their mean duration of hospital stay was 9.9 days (P value = 0.511, not significant). These results reveal that the HbA1c didn't have the correlation with mean duration of hospital stay in DKA patients.

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RESULTS

Table: 1- Age distribution in DKA patients

s.no	Patients age in years	No of DKA patients	Mean age in years	Percentage (%)
1	13- 30	7	16.2	14
2	21-30	13	26.02	26
3	31-40	11	33.14	22
4	41-50	6	45.08	12
5	51-60	8	54.04	16
6	More than 60	5	68.20	10

Chart: 1

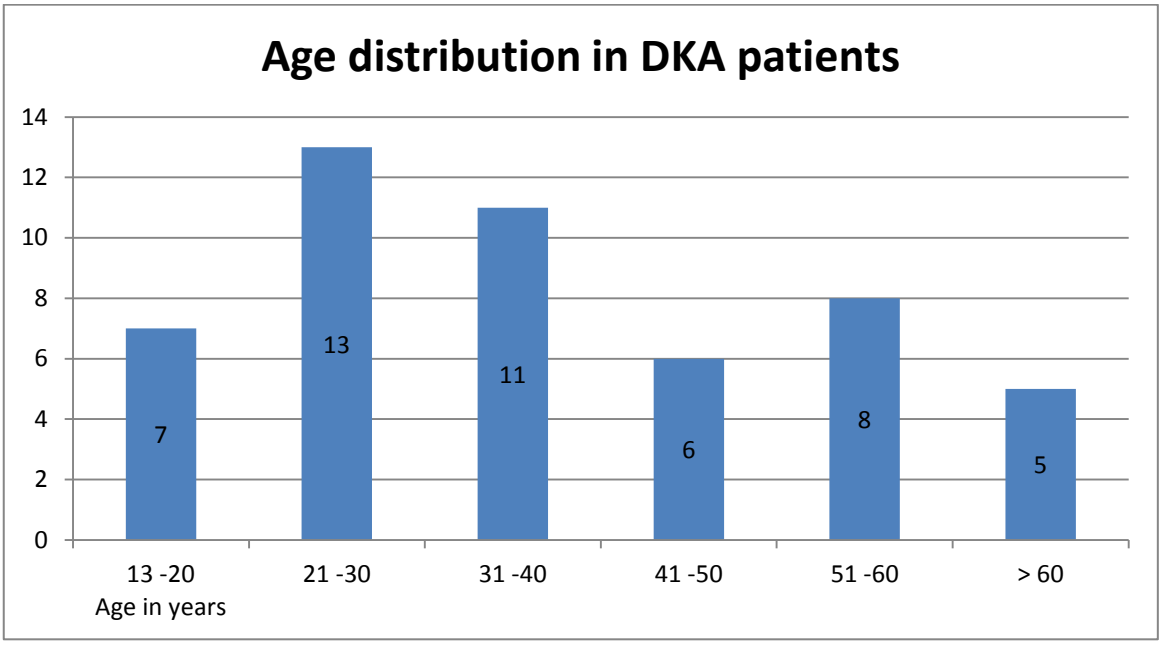

Age distribution in DKA patients
14
12
10
8
6
4
2
0
7
13
11
6
8
5
13 -20
21 -30
31 -40
41 -50
51 -60
> 60
Age in years

Table: 2 - sex distribution in DKA patients

S.no	sex	No of DKA patients	Percentage (%)
1	Male	36	72
2	Female	14	28
total		50	

Chart: 2

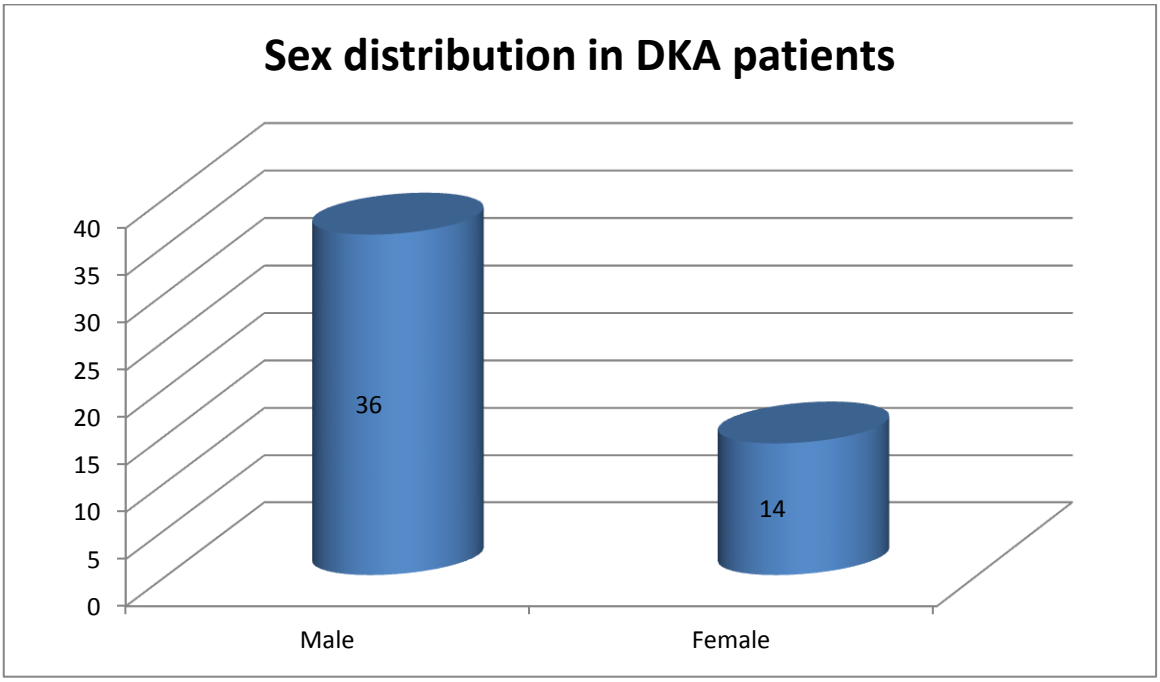


Table : 3

s.no	Type of diabetes	No of DKA patients	Percentage
1	Type 1	31	62
2	Type2	19	38
total		50	

Chart-3

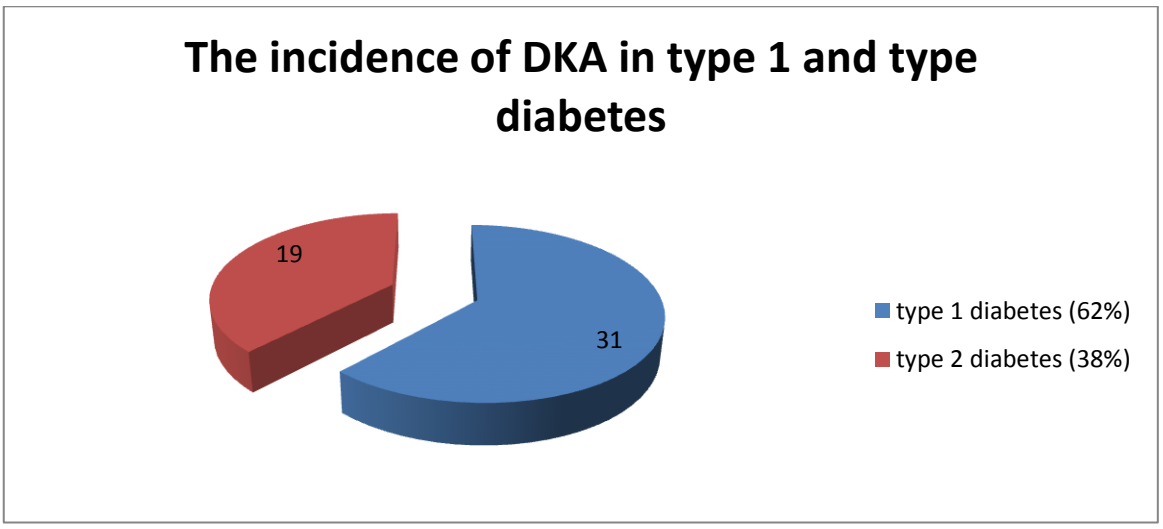
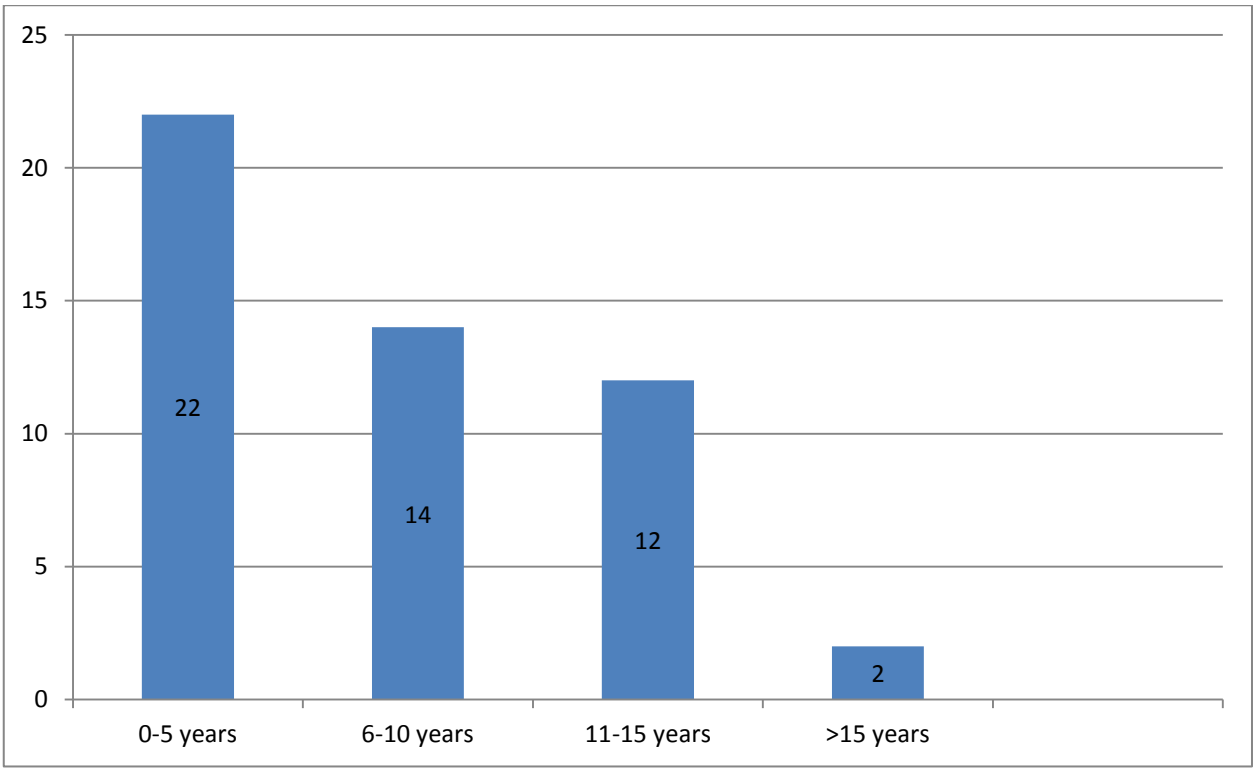


Table- 4

S.no	Duration of diabetes in years	No of DKA patients	Percentage (%)
1	0-5	22	44
2	6-10	14	28
3	11-15	12	24
4	>15	2	4

Chart – 4

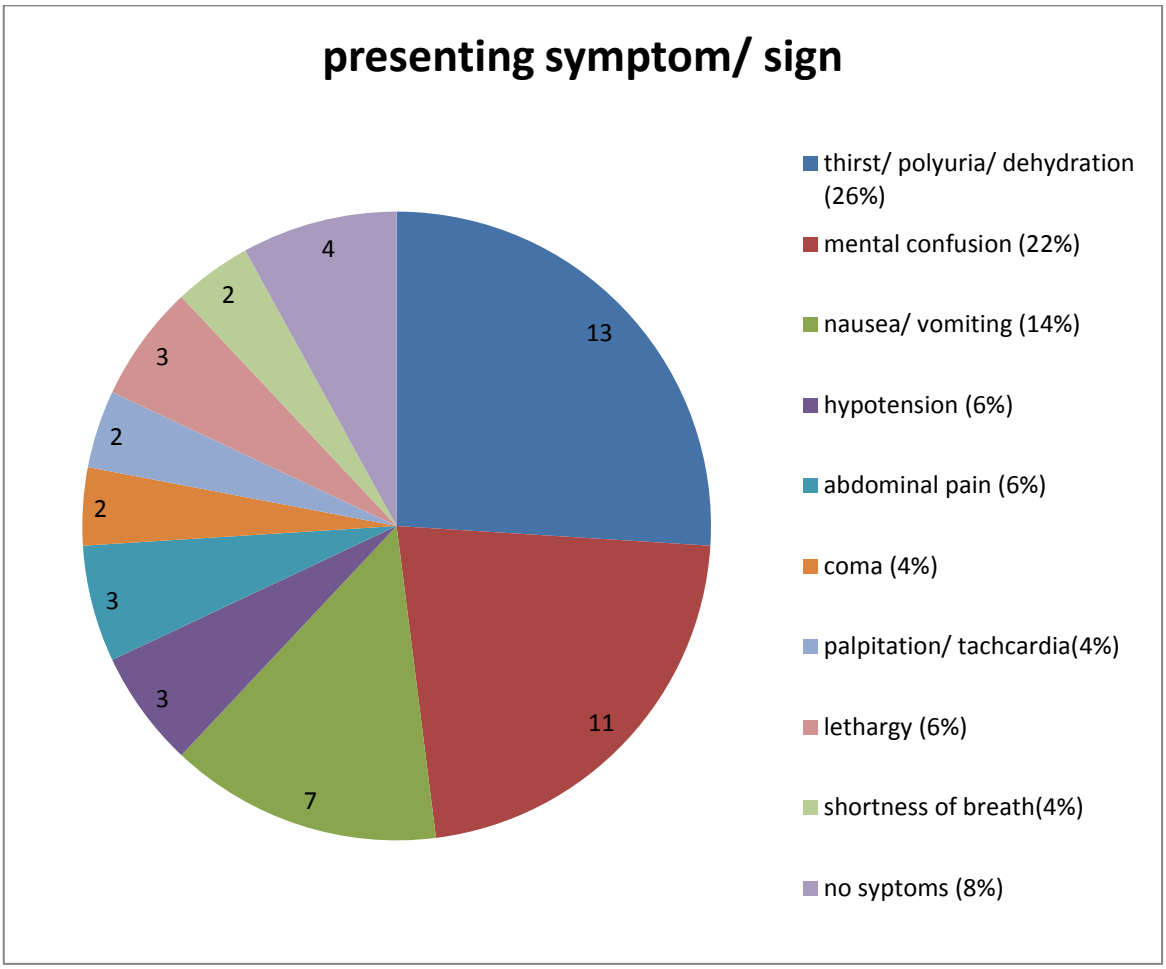


Duration of diabetes and incidence of DKA

Table – 5

S.no	Presenting symptom/ sign	No of DKA patients	Percentage (%)
1	Thirst/polyuria/ dehydration	13	26
2	Mental confusion	11	22
3	Nausea/vomiting	7	14
4	Hypotension/cold extremities	3	6
5	Shortness of breath	2	4
6	Abdominal pain/ discomfort	3	6
7	lethargy	3	6
8	Palpitation/ tachycardia	2	4
9	coma	2	4
10	No symptoms	4	8
	Total	50	

Chart - 5



Thirst, polyuria with dehydration, mental confusion and nausea, vomiting were identified in more patients.

Table – 6

S.no	Precipitating cause	No of DKA patients	Percentage (%)
1	Infection	17	34
2	Insulin/ OAD omission	14	28
3	Inadequate insulin administration	7	14
4	Infarction	2	4
5	No cause identified	8	16
6	newly diagnosed DM presenting with DKA	2	4

Chart -6

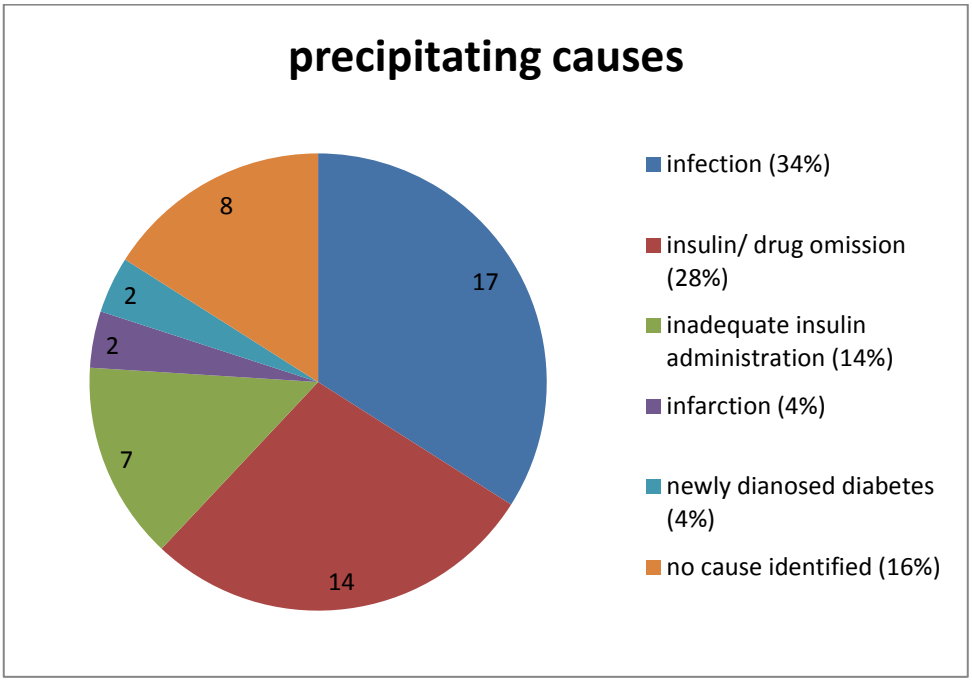


Table -7

S.no	HbA1c level	Number of DKA patients	Percentage (%)
1	6.5 -7.5	5	10
2	7.6 -8.5	9	18
3	8.6 – 9.5	12	24
4	>9.6	24	48

Chart -7

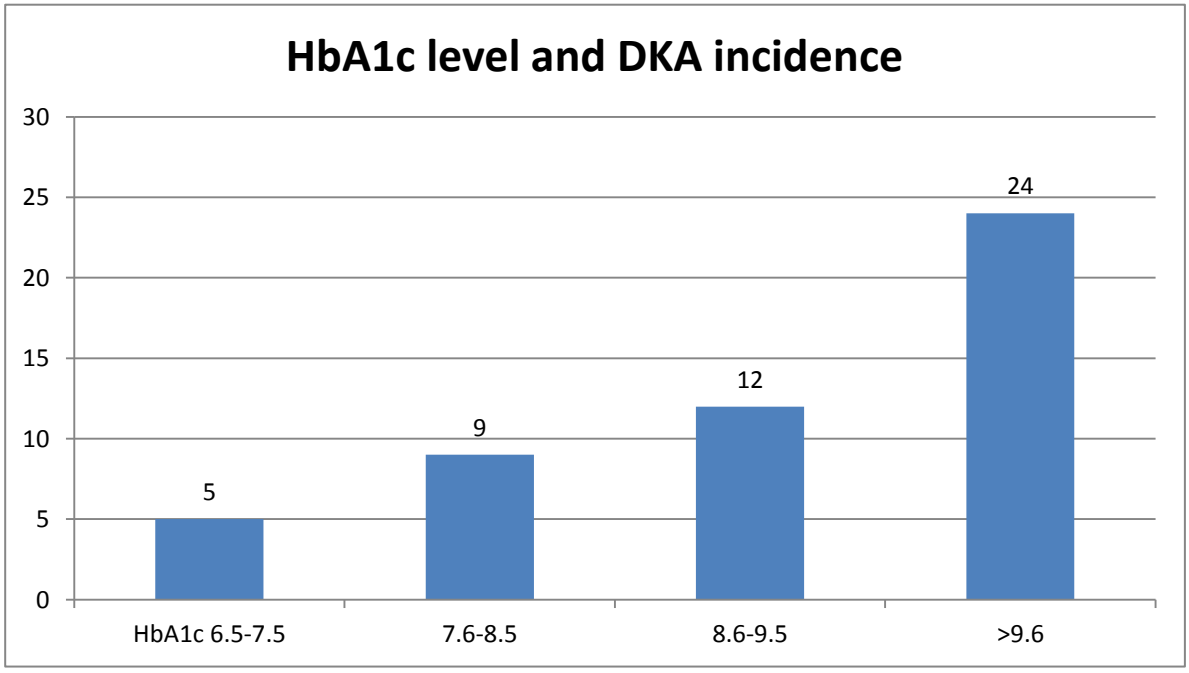
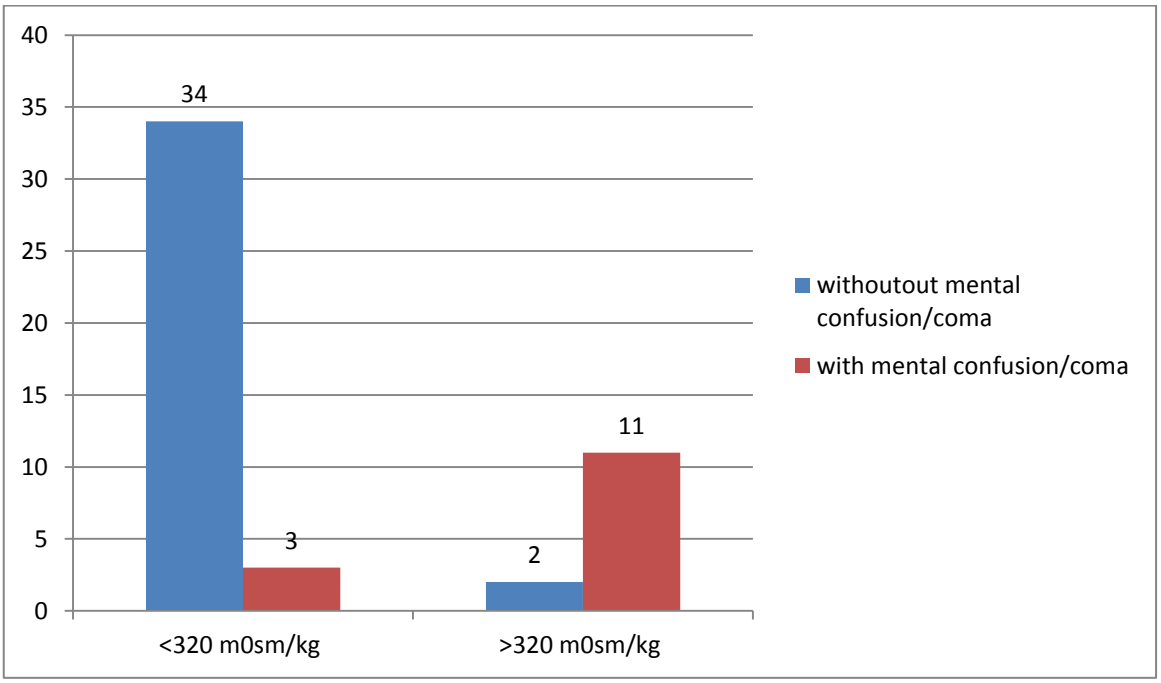


Table - 8

s.no	Serum osmolality (m0sm/kg)	No of DKA patients	No of DKA patients with mental confusion/ coma	Percentage (%)
1	<320	37	3	8.1
2	>320	13	11	84.6
total		50	14	

Chart - 8

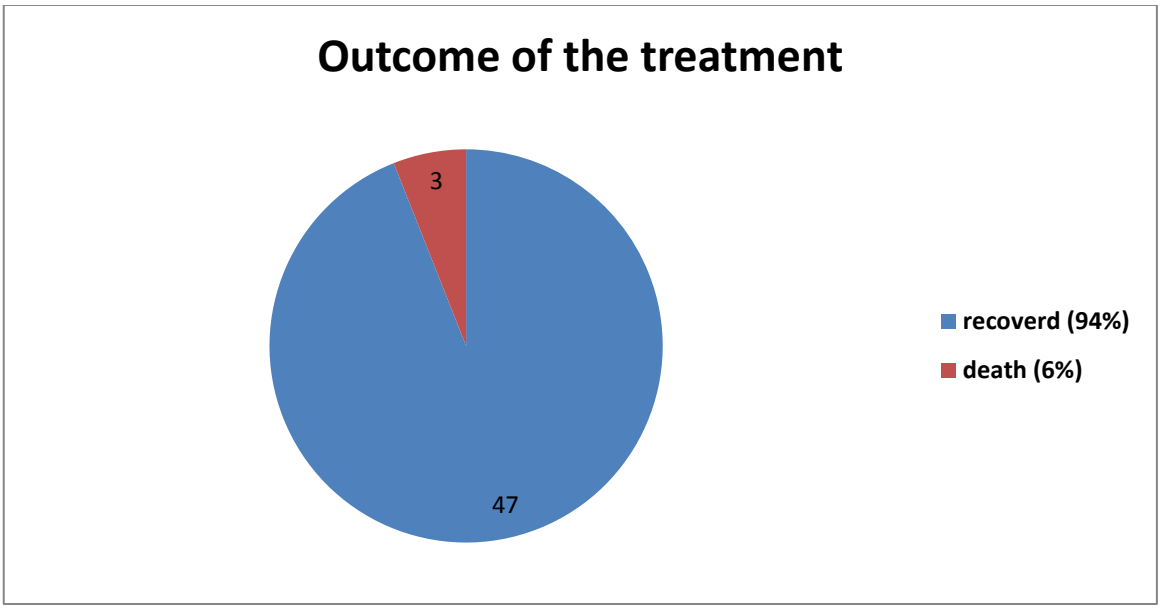


Correlation of patient's serum osmolality and their presentation with mental confusion in DKA.

Table – 9

S.no	Outcome of the treatment	No of DKA patients	Percentage (%)
1	Recovered	47	94
2	Death	3	6

Chart -9



During hospital treatment, among 50 DKA patients, 47 patients recovered completely and 3 patients died due to complications.

Table – 10

s.no	Serum bicarbonate level in mEq/ L	No of DKA patients	Mean duration of hospital stay	P value
1	16- 20	31	9.8 days	0.054
2	11- 15	12	12.06 days	0.004
3	< 10	7	14.2 days	0.001
total		50		

Chart -10

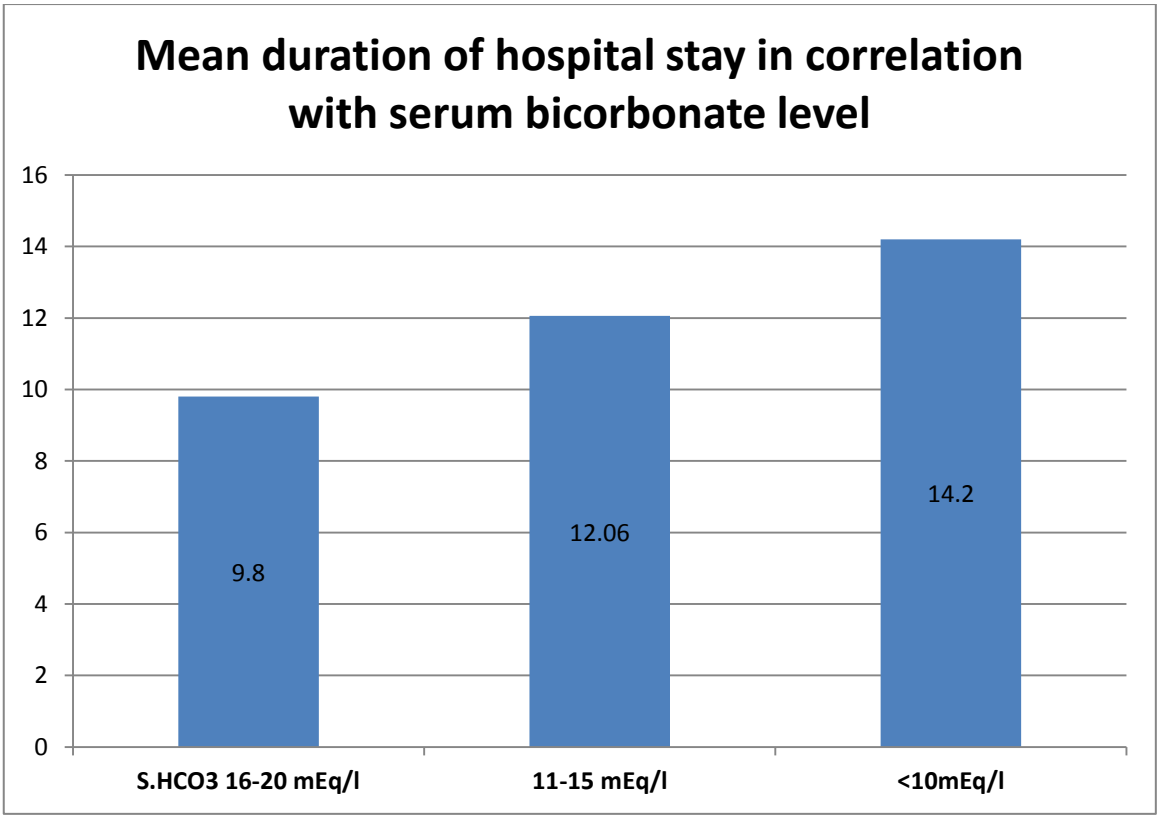
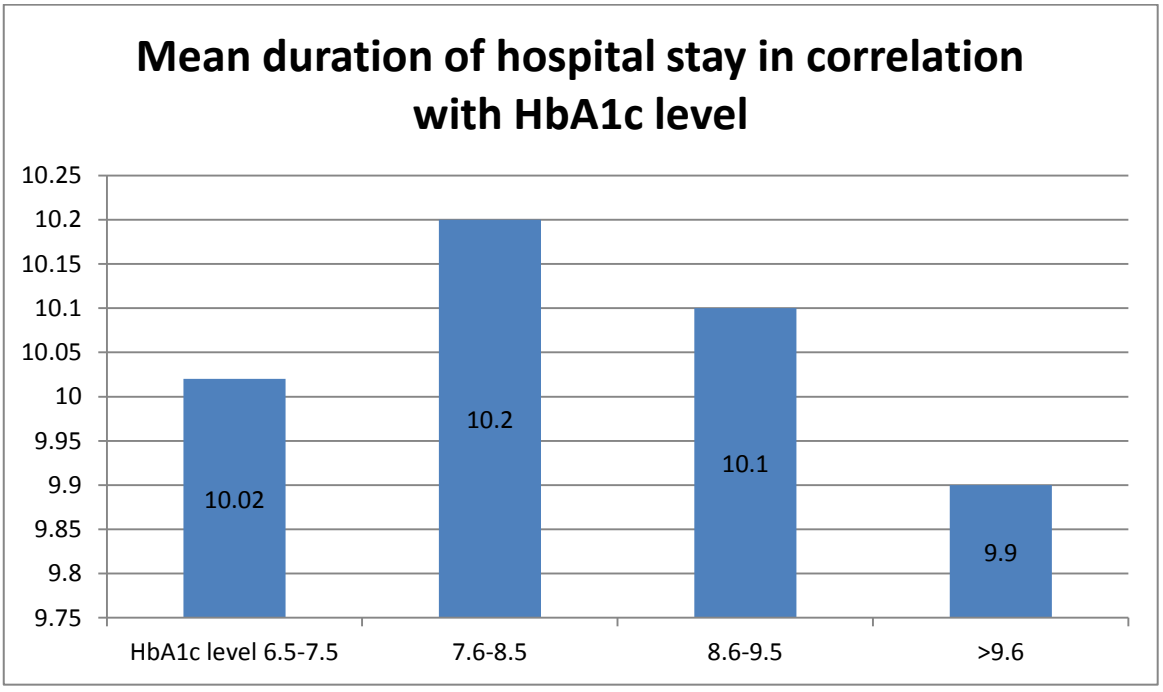


Table - 11

s.no	HbA1c level	No of DKA patients	Mean duration of hospital stay in days	'p' value	Statistical significant
1	6.5 -7.5	5	10.02	0.504	Not significant
2	7.6 -8.5	9	10.2	0.482	Not

					significant
3	8.6 – 9.5	12	10.1	0.501	Not significant
4	>9.6	24	9.9	0.511	Not significant
total		50			

Chart – 11



DISCUSSION

AGE DISTRUBUTION:

In this study, more incidence of Diabetic occurs in the 20 – 40 age groups in adult population. This finding was consistent with a study a conducted by Balasubramanyam A et al.

SEX DISTRIBUTION:

In our study, males were 36 and females were 14. Male: female ratio was 2.6: 1. It is comparable with studies done by Berhane Seyoum, MD University school of Medicine, Detroit. In his study, he observed that the male: female sex ratio was 2:1.

INCIDENCE OF DKA IN CORRELATION WITH TYPE OF DIABETES:

In our study, among these 50 patients, 31 (62%) were type 1 diabetes and 19 (38 %) were type 2 diabetes. This result was correlating with studies conducted by Wachtel Tj et al. Diabetic ketoacidosis was more common among the type 1 diabetics.

CORRELATION OF DURATION OF THE DIABETES AND THE INCIDENCE OF DKA:

In this study, the incidence of DKA was more in early period of diabetes (In 0-5 years duration of Diabetes, 22 patients developed DKA among 50 patients). This clearly showed that the incidence of DKA was not increasing in relation with increased duration of diabetes.

PRESENTATION OF DKA:

In our study, thirst, polyuria with dehydration (26%), mental confusion (22%) and nausea / vomiting (14%) are the most common presentations in DKA. These findings were consistent with the findings in a study done by C Rajasoorya et al.

PRECIPITATING CAUSES IN DKA:

In this study, among the precipitating causes, infection accounts for about 34%, insulin/ drug omission accounts for about 14 %, and inadequate insulin administration accounts for about 7%. These results were comparable with results of studies done by matoo Vk, and Bonadio wa et al.

CORRELATION OF DKA INCIDENCE WITH HbA1c LEVEL:

In our study, among the 50 patients 24 (48%) patients were having the HbA1c level more than 9.6 % and 12 patients (24%) were having HbA1c level in between 8.6 – 9.5 %. This showed that incidence of diabetic ketoacidosis was higher in patients with high HbA1c level. This result was correlating with a study done by Ramaswamy Ganesh at Baylor college of Medicine, Houston. In his study, he observed that all the 21 patients were having high HbA1c values.

SERUM OSMOLALITY AND DKA PRESENTATION – CORRELATION:

In our study, out of 50 patients , 37 patients were having serum osmolality values less than 320mOsm/kg and 13 patients were having more than 320 mOsm/ kg. Among these 37 patients, only 2 (8.1%) were presented with mental confusion/coma but, but in second group, among 13 patients, 11 patients (84.6%) were presented with mental confusion / coma. This clearly indicates that the patient's serum osmolality was strongly correlates with their mental state. These findings were similarly coincides with a study done by C Rajasoorya and his colleagues; among 33 DKA patients in Department of medicine, Alexander hospital, Singapore and references in the standard text book.

OUTCOME OF THE DKA DURIGNG TREATMENT:

In this study, out of 50 patients, 47 (94%) were cured and 3 (6%) patients died due diabetic ketoacidosis complications. The mortality rate was 6%. This result is consistent with findings in the various studies. Berhane Seyoum, MD, University school of Medicine, Detroit, did a study in 847 DKA patients; the mortality rate in his study was 6 %.

CORRELATION OF SERUM BICORBONATE LEVEL AND MEAN DURATION OF HOSPITAL STAY:

In this study, out of 50 patients, 31 patients were having their serum bicarbonate level, in between 16-20 mEq/l and mean duration of hospital stay in these patient was 9.8 days (p value = 0.054; statistically not significant). twelve patients were having serum bicarbonate values in between 11-15 mEq/l and the mean duration of hospital stay in these patients was 12.06 days (p value = 0.004; statistically significant). Seven patients were having the serum bicarbonate values less than 10 mEq/l and the mean duration of hospital stay in these patients was 14.2 days (p value = 0.001; statistically significant). This results clearly shows, when the serum bicarbonate level decreases, the degree

of metabolic acidosis also increases and affects the outcome of the DKA patients; these findings were coincides with references in the standard text books.

HbA1c LEVEL AND MEAN DURATION OF HOSPITAL STAY-CORRELATION:

In this study, the mean duration of hospital stay was almost equal in all groups with various HbA1c levels. The values are not statistically significant. These results show that HbA1c level didn’t have any correlation with the outcome of the DKA patients.

LIMITATIONS OF THE STUDY

1. In this study, urine acetone was used as a diagnostic method to detect ketoacidosis. Plasma ketone estimation was not done.
2. Small number of population was taken as study subjects.
3. Diabetic ketoacidosis patients were not followed after the study period.

CONCLUSION

1. Diabetic ketoacidosis incidence is more in 20-40 years age group in adult population.

2. Diabetic ketoacidosis is more often occur in males compare to females.

3 .The incidence of the DKA is more in Type 1 diabetic compare to type 2 diabetics.

4 .Duration of diabetes doesn't have any correlation with incidence of diabetic ketoacidosis.

5. Thirst, polyuria with dehydration, mental confusion, and nausea/ vomiting are the common presentation this study.

6. Infection, insulin/ drug omission, and inadequate insulin administration are more frequently noticed precipitating factors in this study.

7. HbA1c level have a positive correlation with the incidence of DKA.

8. Patient's high serum osmolality value is strongly associated with their presentation of mental confusion/coma.

9. The mortality rate in this study is 6 %.

10. Patient's low serum bicarbonate level is strongly associated with their prolonged stay in the hospital.

11. Patient’s HbA1c level doesn’t have any correlation with their stay in the hospital.

PROFORMA

NAME:

AGE:

SEX:

ADDRESS:

TYPE OF DIABETES:

DURATION OF DIABETES:

PRESENTATION:

Nausea/ vomiting □ Mental confusion □

Thirst / polyuria □ Coma □

Weight loss / weakness □ without symptoms □

Abdominal pain □ Hypotension □

PRECIPITATING CAUSE :

In adequate insulin administration □

Poor patient compliance □

Infection □

Infarction □

No obvious precipitating cause □

BIOCHEMICAL PROFILE :

Random blood sugar**:**

Blood Urea:

Serum Creatinine:

Serum electrolytes:

Sodium:

Potassium:

Bicarbonate:

HbA1c level:

Urine acetone:

Serum osmolality:

OUTCOME:

Recovered □

Death □

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S.N	A	S	TYPE	RBS	UREA	C	NA	K	HCO 3	HbA1C	OSM	UA	D	SYM	P.F	O
1	66	F	type 2	600	196	2.7	144	5.2	15.5	8.2	356.5	P	20	mental confusion	infection	R
2	36	M	type1	543	60	1.3	149	3.8	9.6	9.9	338.9	P	1	coma	subdural hematoma	D
3	29	M	type1	466	52	1.2	139	4.3	17.2	8.4	322	P	5	mental confusion	insulin omission	R
4	80	M	type 2	455	71	1.4	151	5.4	19	9	351	P	30	coma	no cause	R
5	29	M	type1	322	77	1.2	139	4.8	18.5	9.2	303	P	5	nausea/vomiting	insulin omission	R
6	49	F	type2	445	54	1.8	134	4.7	18.1	6.8	310	P	6	thirst/ polyuria	infection	R
7	56	M	type2	356	43	1.1	129	5.2	16.4	7.4	301	P	13	Hypotension& cold extremities	infection	R
8	48	M	type2	476	40	0.9	155	5.1	20	7.1	344	P	11	mental confusion	drug omission	R
9	23	F	type 1	487	34	0.8	126	5.6	14.8	8.9	308	P	5	abdominal pain	drug omission	R
10	34	M	type1	478	50	0.8	131	4.5	9.2	9.2	298	P	13	dehydration	insulin omission	R
11	58	M	type2	390	45	0.7	154	5	18.4	11	338	P	10	nausea/vomiting	infection	R
12	38	M	type 1	376	32	0.9	126	5.4	15.6	10.2	303	P	15	acidotic breathing	no cause	R
13	18	M	type 1	410	49	1.3	131	5.1	17.4	9.3	300.5	P	4	dehydration	newly diagnosed	R
14	34	F	type 1	476	32	1.2	129	4.4	9.4	10	291	P	3	thirst/ polyuria	drug omission	R
15	57	M	type2	511	65	1.4	144	4	17.3	10.5	301.5	P	8	dehydration	infection	R
16	61	M	type2	466	43	1	144	4.6	12.4	7.8	288	P	11	no symptoms	no cause	R
17	49	F	type2	473	42	1.4	134	5.4	14.5	9.2	313	P	4	mental confusion	infection	R
18	19	M	type 1	398	32	1	148	5.1	18	9.6	324	P	4	mental confusion	insulin omission	D
`19	33	F	type 1	455	37	0.8	131	4.9	15	8.2	307	P	8	dehydration	insulin omission	R
20	36	M	type 1	490	35	1.1	137	3.5	9.5	10.1	300.5	P	11	mental confusion	no cause	R
21	27	F	type 1	481	33	1.2	134	2.9	15.1	8.5	315	P	5	acidotic breathing	infection	R
22	58	M	type2	394	35	1	131		14	9.1	291	P	11	dehydration	drug omission	R
23	48	M	type2	600	37	1.3	129	5.1	19	9.7	301.5	P	4	dehydration	no cause	R
24	31	F	type1	543	51	1.7	136	4.4	16.4	9	288	P	9	nausea/vomiting	infection	R
25	51	M	type2	466	71	1.9	143	4	10	10.2	313	P	4	dehydration	infection	R

Sn	A	S	TYPE	RBS	U	Cr	NA	K	HCO	HbA1C	OSM	U.A	D	SYMPTOM	P.F	O
26	21	M	type 1	455	50	1	155	4.6	17	7.4	343	P	2	mental confusion	insulin omission	R
27	16	M	type 1	322	44	1.1	151	5.4	19	7.1	329	P	4	mental confusion	infection	R
28	36	M	type2	445	33	0.9	131	5.1	16.3	8.9	291	P	10	dehydration	drug omission	R
29	46	F	type2	356	32	0.7	134	4.9	18	9.2	301.5	P	3	lethargy	inadequate insulin	R
30	60	M	type2	476	32	1.2	126	3.5	19.2	11	288	P	8	thirst/ polyuria	infection	R
31	22	M	type 1	487	30	1	131	4.8	18	10.2	313	P	5	tachycardia	no cause	R
32	28	M	type 1	478	29	0.9	144	3.8	21	9.3	327	P	6	mental confusion	insulin omission	R
33	20	M	type 1		78	2.1	155	4.3	9.6	8	344	P	3	mental confusion	inadequate insulin	R
34	33	F	type1	376	31	0.8	129	5.4	17	7.8	298	P	9	lethargy	no cause	R
35	43	M	type2	410	28	1.2	118	4.8	13	7.8	301	P	4	nausea/vomiting	infection	R
36	58	M	type2	476	25	0.8	129	4.7	17.2	8.2	308	P	12	hypotension	infection	R
37	18	M	type 1	511	65	1.2	144	5.2	18	9.9	318	P	1	dehydration	no cause	R
38	34	M	type 1	466	32	1.2	143	5.1	17.2	8.4	303	P	12	nausea/vomiting	insulin omission	R
39	16	F	type 1	473	75	2.3	152	5.6	19	9	345	P	3	dehydration	newly diagnosed	R
40	17	M	type1	398	49	0.8	134	4.5	18.5	9.2	304	P	3	dehydration	infection	R
41	25	F	type 1	455	54	1.2	131	5	18.1	6.8	297	P	7	abdominal pain	infection	R
42	31	M	type 1	490	76	2	134	5.4	16.4	7.4	309	P	9	lethargy	infection	R
43	28	M	type 1	481	40	2.9	126	5.1	20	7.1	301	P	5	tachycardia	inadequate insulin	R
44	29	F	type 1	394	24	0.8	151	4.4	14.8	10.6	327	P	9	altered sensorium	cerebral infarction	D
45	20	M	type 1	480	55	2.6	152	4	19	9.2	306	P	4	mental confusion	insulin omission	R
46	57	M	type2	511	76	1.7	129	4.6	18.4	11	291	P	12	hypotension	infection	R
47	63	F	type2	385	100	2	136	5.4	9.8	10.2	301.5	P	13	no symptoms	drug omission	R
48	32	M	type 1	411	23	0.8	131	5.1	17.4	9.3	288	P	12	lethargy	insulin omission	R
49	21	M	type 1	470	71	1.9	126	4.9	13.2	8	313	P	4	dehydration	inadequate insulin	R
50	20	M	type 1	385	34	0.8	131	3.5	17.3	9.5	306	P	6	no symptoms	infection	R

SN- SERIAL NUMBER

A- AGE

S- SEX

M-MALE

F-FEMALE

RBS- RANDOM BLOOD SUGAR

U-UREA

CR-CREATININE

NA-SODIUM

K-POTASSIUM

HCO-BICORBONATE

OSM-SERUM OSMOLALITY

U.A-URINE ACETONE

D-DURATION OF DIABETES

PF-PRECIPITATING FACTOR

O-OUTCOME

R- RECOVERED

D- DEATH